

THE CLINICAL PULMONARY INFECTION SCORE (CPIS) IN THE DIAGNOSIS OF VENTILATOR ASSOCIATED PNEUMONIA (VAP) IN INTENSIVE MEDICAL CARE UNIT AT TERTIARY CARE HOSPITAL

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Abstract

Background: Ventilator-associated pneumonia (VAP) is a pneumonia that develops at least 48 hours after invasive mechanical ventilation in patients without clinical findings supporting the development of pneumonia or pneumonia during intubation. Clinical pulmonary infection score (CPIS) as a screening tool in ventilator-associated pneumonia (VAP). **Objective:** Ventilator-associated pneumonia (VAP) is one of the leading nosocomial infections in intensive care units (ICUs), causing high mortality and increased health care costs. It is known that early diagnosis and treatment reduce mortality and morbidity. In this study, we aimed to assess the efficacy of the Clinical Pulmonary Infection Score (CPIS) in early diagnosis in VAP. **Materials and Methods:** We conducted the study on 50 cases. Clinical Pulmonary Infection Score parameters of each patient-body temperature, leukocyte count and morphology, volume and character of tracheal secretions, arterial oxygenation, pulmonary infiltration on a chest X-ray, progression of pulmonary infiltration, and microbiological culture results-were recorded. When the patient was admitted, the first five parameters of CPIS were used to make the scores. After 48 hours, seven parameters were used along with the tracheal aspirate (TA) culture results to make the scores after the intubation. We followed the patients by calculating the CPIS during the mechanical ventilation and obtaining tracheal aspirate (TA) cultures every three days. We grouped the patients as VAP (+) and VAP (-) based on the obtained data. **Result:** Baseline CPIS values were between 0 and 5, with a mean value of 3.39 ± 1.10 . The 48th-hour CPIS values of the cases were between 1 and 10, with a mean value of 4.41 ± 1.85 . Intensive care entry basal CPIS levels were found to be 3.42 ± 1.20 in cases with VAP and 3.48 ± 1.10 in cases with no VAP, with no significant difference between them ($p=0.795$). There was a statistically significant difference between the 48-hour CPIS and 5th-day CPIS values of VAP (+) and VAP (-) cases ($p<0.001$). There was a difference between the pre-diagnosed CPIS levels of VAP (+) and VAP (-) cases ($p<0.001$). **Conclusion:** Serial CPIS measurements can help the clinician in early diagnosis and treatment of VAP.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a pneumonia that develops at least 48 hours after invasive mechanical ventilation in patients without clinical findings supporting the development of pneumonia or pneumonia during intubation.^[1] VAP is a common nosocomial infection in intensive care

units (ICUs), and its results can be listed as high mortality, prolonged intensive care stay, and increased health care cost.^[2, 3] High-risk bacteria causing VAP, previous antibiotic and H2-blocker drug use of the patient, follow-up APACHE II (Acute Physiology and Chronic Health Evaluation) score greater than 20, high creatinine levels, bacteraemia, organ failure, and premorbid lifestyle score of 2 or higher increase VAP-associated

mortality.^[4,5] VAP accounts for more than half of all antibiotic use in the ICU.^[6] As a result, VAP causes significant morbidity and financial consequences.^[7, 8] Because of these reasons, early diagnosis and treatment of VAP are critical.

Despite its high incidence, diagnosis is very difficult due to the presence of similar clinical findings in many patients in the intensive care unit. A weak link was found between the clinical diagnosis of pneumonia and true pneumonia in the multiple patient series. It was also said that half of the patients labelled as VAP were not actually sick and one-third of the VAP patients could not be located [9]. In order to make a simple tool for diagnosing

VAP, a scoring system with 7 clinical parameters for VAP diagnosis. We named the system the Clinical Pulmonary Infection Score (CPIS) (Table-1) [9, 10]. This scoring system evaluates the clinic using radiological and endotracheal aspirate (ETA) culture results. The diagnosis of VAP was made using body temperature, leucocyte count and morphology, tracheal secretion amount and character, PaO₂ / FIO₂ ratio, presence of pulmonary infiltration and its progression, and microbiological culture results. A score of 6 or more suggests VAP. In our study, we aimed to investigate the efficacy of the CPIS as a screening tool for the early diagnosis of VAP.

Table-1: Clinical Pulmonary Infection Score (CPIS)^[9, 10]

| Parameters | CPIS |
|--|---|
| Body temperature | ≥ 36.5 or ≤ 38.4 = 0 point |
| | ≥ 38.5 or ≤ 38.9 = 1 point |
| | ≥ 39 or < 36.5 = 2 point |
| Leukocyte count, microscopy | ≥ 4000 or ≤ 11.000 = 0 point |
| | < 4000 or > 11.000 = 1 point |
| | Rod form ≥ % 50 = Add 1 point |
| Tracheal secretion | Tracheal secretion (-) = 0 point |
| | Tracheal secretion with less purulence = 1 point |
| | Abundant purulent secretion = 2 points |
| Oxygenization | PaO ₂ / F _I O ₂ , mmHg > 240 or ARDS (ARDS: PaO ₂ / F _I O ₂ < 200, PaO ₂ / F _I O ₂ < 200, PAWP ≤ 18 mmHg and bilateral acute infiltration) = 0 point |
| | PaO ₂ / F _I O ₂ , mmHg ≤ 240 or ARDS = 2 points |
| | |
| Pulmonary infiltration in chest X-ray | No infiltration = 0 point |
| | Diffuse infiltration = 1 point |
| | Localized infiltration = 1 points |
| Progression in pulmonary infiltration | Radiographic progression (-) = 0 point |
| | Radiographic progression (+) (After the exclusion of HF and ARDS) = 2 points |
| Pathogenic bacteria in tracheal aspirate culture | No or few pathogenic bacteria = 0 point |
| | Moderate or high levels of pathogenic bacteria = 1 point |
| | Pathogenic bacteria to be seen in Gram staining, add 1 point |

Total (>6 are accepted as pneumonia); ARDS: acute respiratory distress syndrome; HF: heart failure; PAWP: pulmonary artery wedge pressure

MATERIALS AND METHODS

This study was conducted in the ICU, after the approval of the Ethical Committee of Fathima Institute of Medical Sciences, Kadapa. We obtained written informed consent from the patient. Study duration one year period (March 2023– February 2024), on 50 subjects aged between 20 and 80 years with a median age of 67.82±9.86 years who met the inclusion criteria for the study.

A total 356 patients were followed up in ICU, and patients who had mechanical ventilator support for longer than 48 hours were included in the study. Patients with pneumonic infiltration during intubation, patients with a sepsis diagnosis, immunocompromised patients with a viral disease, patients receiving chemotherapy and/or radiotherapy, and patients who were intubated for less than 48 hours were excluded from the study.

We recorded the patients' age, gender, intensive care entry diagnoses, systemic diseases, and APACHE II scores. After the patients were intubated, their body temperature, leukocyte counts and morphology,

tracheal secretions and volumes, and blood gas results were all recorded. Posteroanterior (PA) chest graphics were also taken. We took endotracheal aspiration (ETA) specimens using a closed system, safeguarding them from contamination under sterile conditions, and utilizing a Lukens Specimen Container. The ETA sample was sent to the microbiology laboratory for gram staining and culture under appropriate conditions.

Microbiological processes: The samples were delivered to the microbiology laboratory within 30 minutes after collection. 1 ml of ETA was mixed with 1 ml of physiological saline and mechanically crushed for 1 minute, then cultivated into 100 µl of 5% sheep blood agar, chocolate agar, and Mac Conkey agar. Microscope slides were prepared for Gram staining. ETA slides were scored as 0, +1, +2, and +3 according to the Q scoring system.^[9, 11] Chocolate-coated agar plates were incubated at 35°C in 5-10% CO₂ in the sterilizer. 5% sheep blood agar and chocolate-coated agar were incubated for 48 hours before evaluation. We calculated breeding based on literature knowledge

by quantifying (colony number) x (dilution rate)-1 X 10.^[12-14] The literature once again recognized ETA as a positive reproduction over 10*5 cfu/ml.^[15, 16] The Mini Api (Biomérieux) system performed the identification.

We recorded CPIS parameters for each patient. They looked at things like; body temperature, leucocyte count and morphology, tracheal secretion volume and character, PaO₂/F_IO₂ values, presence of pulmonary infiltration, pulmonary infiltration progression, and microbiological culture results were recorded. VAP was diagnosed according to the results of ETA culture, taking clinical findings and chest X-ray into account and was confirmed by the “Infectious Diseases Committee,” which was formed by experts on the subject. The patient's CPIS values were found at the time of admission by looking at five things: body temperature, the number and shape of white blood cells, the amount and type of tracheal secretions, the patient's PaO₂/F_IO₂ values, and the presence of pulmonary infiltration. These values were kept until the gram staining and culture results were available. This value was accepted as basal CPIS. We found the CPIS values 48 hours after the intubation by looking at seven things: body temperature, the number and shape of white blood cells, the amount and type of tracheal secretions, the PaO₂/F_IO₂ levels, the presence of pulmonary infiltration, the progression of pulmonary infiltration, and the results of microbiological cultures. Next, we collected ETA samples at intervals of 3 days. We obtained the culture results two days after taking the samples. These results guided the diagnosis of VAP. We also calculated the CPIS values of patients who did not receive a VAP diagnosis and were still under monitoring based on these culture results. We

followed up with patients at 3-day intervals (48th hour, 5thday, 8thday, 11th day, 14thday) and calculated their CPIS values. Patients were divided into two groups as VAP (+) and VAP (-).

Statistical Analysis

Statistical analyses were done using SPSS for Windows software (version 22; SPSS Inc., Chicago, IL, USA). For parametric tests, descriptive statistical values were given as mean and standard deviation. For non-parametric tests, they were given as median, minimum, and maximum values. For categorical data, they were given as frequency and ratio. Student's t-test and paired t-test were used to compare variables. The Mann-Whitney U test was used to compare percent changes between measurements. Significance was assessed at the p<0.05 level.

RESULTS

The study was conducted within 12 months on 50 subjects aged between 20 and 80 with a mean age of 67.82 ± 9.86 years. Of the 356 patients followed in the ICU during the study period, 305 were excluded from the study due to sepsis, malignancy, diagnosis of pneumonia at admission, and/or mechanical ventilator support for less than 48 hours. 42% of the cases (n=21) were women, and 58% (n=29) were male subjects. There were a total of 12 (24 %) cases of ischemic stroke, 16% of which were after CPR, 18% of which had pulmonary edema, 32% of which had respiratory failure, and 8% of which had multiple organ trauma. Brain malignancy was found in 4% of the cases. Table 2 displays the baseline demographic data.

Table 2: Baseline demographic data

| Variable | Mean (SD) or Percent (N= 50) |
|------------------------------|------------------------------|
| Age, year | 67.82 ± 9.86 |
| Gender | |
| Male | 29 (58%) |
| Female | 21 (42%) |
| Distribution of cases | |
| brain malignancy | 2 (4%) |
| gastrointestinal bleeding | 5 (10%) |
| hemorrhagic stroke | 4 (8%) |
| hepatorenal syndrome | 2 (4%) |
| ischemic stroke | 12 (24%) |
| post-CPR | 8 (16%) |
| pulmonary edema | 9 (18%) |
| respiratory failure | 16 (32%) |
| multiple organ trauma | 4(8%) |

Baseline CPIS values were between 0 and 5, with a mean value of 3.39 ± 1.10. The 48-hour CPIS values of the cases were between 1 and 10, with a mean value of 4.41 ± 1.85. According to the 48-hour culture results, 12 of the patients received a VAP diagnosis. After 48 hours, we discharged 5 of the cases and continued to monitor 33 others. We evaluated the fifth- day CPIS value in 33 cases. The CPIS values of 33 patients were between 1 and 11,

with a mean value of 4.90 ± 2.20. According to the culture results on 5th day, 8 of the cases received a VAP diagnosis. The 5th day saw the discharge of 8 out of 33 cases, the death of 6 cases, and the continued monitoring of 10 cases. On day 8, CPIS was assessed in 10 cases. The CPIS values were found to range from 2 to 9 with a mean value of 4.50 ± 1.50. According to culture results on day 8, one of the patients received a VAP diagnosis. After

the 8th day, 4 of 10 patients were discharged, 5 died, and 1 patient continued to be followed up. The 11th day of this case yielded a CPIS score of 5. The 14th day of CPIS value of this case under on-going

follow-up was 6. The culture result confirmed the diagnosis of VAP for the patient on the 14th day. Table 3 displays the distribution of cases based on CPIS values.

Table-3: Distribution of CPIS Values

| | n | CPIS | | VAP | Dead | Discharged |
|----------------------------|----|---------|-------------|-----|------|------------|
| | | Min/Max | Mean ± SD | | | |
| Basal CPIS | 50 | 0-5 | 3.39 ± 1.10 | - | - | - |
| 48 th hour CPIS | 50 | 1-10 | 4.41 ± 1.85 | 12 | - | 5 |
| 5 th day CPIS | 33 | 1-11 | 4.90 ± 2.20 | 8 | 6 | 8 |
| 8 th day CPIS | 10 | 2-9 | 4.50 ± 1.50 | 1 | 5 | 4 |
| 11 th day CPIS | 1 | 5 | 5.00 ± 1.20 | - | - | - |
| 14 th day CPIS | 1 | 6 | 6.00 ± 1.55 | 1 | - | - |

Intensive care entry basal CPIS levels were found to be 3.42 ± 1.20 in cases with VAP and 3.48 ± 1.10 in cases with no VAP, with no significant difference between them ($p=0.795$). There was a statistically significant difference between the 48th hour CPIS and 5th day CPIS values of VAP (+) and VAP (-) cases ($p<0.001$) (Figure-1).

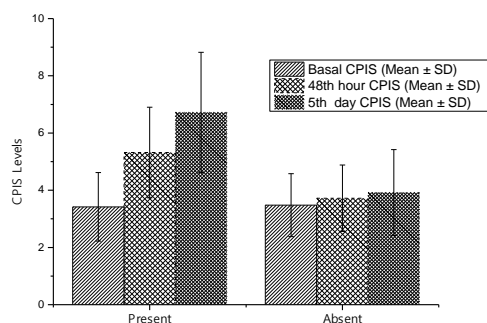


Figure-1: Evaluation of CPIS results at other measurement times according to VAP status and start time

Table-4: Comparison of percentage change values of CPIS measurements in VAP groups

| VAP | Basal 48 th hour % Change Median (min : max) | Basal-5th day % Change Median (min : max) | 48th hour-5th day % Change Median (min : max) |
|---------|--|--|--|
| Present | 0.56 (0:1.00) | 0.89 (0.89:1.62) | 0.72 (0.38:1.46) |
| Absent | 0 (-0.25:0.33) | 0.14 (-0.16:0.39) | 0.01 (-0.17:0.28) |
| P value | 0.128* | <0.001** | <0.001*** |

Mann Whitney U test, * $p<0.05$, ** $p<0.01$

In the VAP (+) cases, CPIS levels before culture outcomes were calculated as 7.82 ± 1.63 , which was significantly higher than VAP (-) cases ($p<0.001$) (Figure-2).

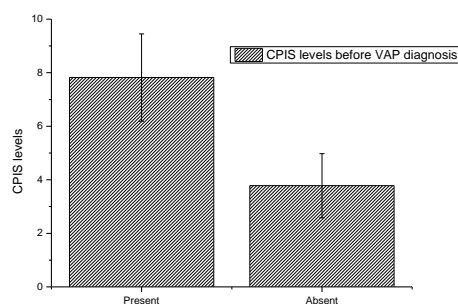


Figure-2: Assessment of CPIS Results before VAP Diagnosis

DISCUSSION

The primary obstacle in VAP diagnosis is the absence of an exact gold standard.^[17] It is usually diagnosed according to clinical, radiological, and microbiological criteria.^[18] Researchers have come up with invasive diagnostic methods (quantitative culture of secretions from the lower respiratory tract obtained by bronchoscopic method).^[19] because they are worried about how inaccurate clinical approaches are in VAP. However, these procedures require strict adherence to bronchoscopic and microbiological techniques, and their place in routine practice is controversial.^[20] The best method for the diagnosis of VAP is to find the earliest and most accurate technique, with the subject still being controversial. Fujitani et al.^[21] attempted to establish a candidate marker of VAP, and they defined the CPIS. This is followed by some studies, not enough in number, about the efficiency of CPIS.

In a retrospective study involving 58 patients with severe brain injury, Pelosi et al. found that CPIS increased from entry to ICU to VAP onset and that CPIS had 97% sensitivity, 100% specificity in VAP diagnosis.^[22] In this study, 50 subjects aged between 20 and 80 with a mean age of 67.82 ± 9.86 years.

In the study of Luna et al., it was observed that the CPIS values increased significantly in the patients until the day of VAP diagnosis. The CPIS value remained high in those who did not survive, while VAP showed a significant decrease in the treatment phase in those who survived. This observation suggests that CPIS correlates with final mortality.^[23] In our study, a statistically significant increase was observed in the CPIS values of patients until the VAP diagnosis. In patients with suspected VAP, the CPIS levels before diagnosis, confirmed by culture results, were found to be significantly higher, and the mean value was found. We observed no increase in CPIS values in VAP cases. There is disagreement about whether a high CPIS value calculated before the culture results should be enough to alert the doctor and be a first sign that antibiotics should be used.

The multicentre randomized VAP diagnostic strategy study by Luyt et al.^[24] found that CPIS>6 correctly identified 89% of VAP patients with bronchoscopy results, but only 47% of them correctly identified the right patients. In this study, The CPIS values of 33 (60%) patients were between 1 and 11, with a mean value of 4.90 ± 2.20 . Based on the microbiological culture results from the third day of this study, it was seen that patients with VAP had higher CPIS values than those without VAP. CPIS values greater than 6 could help find more patients with lung infections. Based on its high sensitivity (89%) and negative predictive value (84%), this clinical scoring has been established as a valid alternative method for reducing the use of antibiotics that aren't needed in people who are suspected of having VAP.

It has been suggested in many studies that the efficacy of CPIS in diagnosing VAP is low; for this reason, it has been investigated in specific patient groups. In the study of Croce et al.^[25] with 158 trauma patients followed by CPIS, no difference was found in terms of bacterial index among patients with CPIS≤6 and CPIS>6. Only 44% of patients with CPIS > 6 had VAP on bronchoalveolar lavage (BAL); 39% of patients with CPIS ≤ 6 were diagnosed with VAP. In the diagnosis of VAP, the sensitivity of CPIS>6 was 61%, and the specificity was 43%. Positive and negative predictive values were 44% and 62%, respectively. In our study, The use of CPIS as a screening in trauma 4 (8%) patients is not thought to help with the final diagnosis process.^[25] The results of this study are controversial because of CPIS>6 being a threshold value for VAP diagnosis and the inflammatory response in trauma patients. 9.3% of our study group consisted of trauma patients, and all of these patients developed VAP. Pham et al. had similar results in the burn patient group. They found that CPIS had poor discriminability, and patients with positive and negative culture results had similar CPIS (mean CPIS of 5, 7, and 5.5, respectively).^[26] Based on the poor sensitivity and specificity of the studies, Zilberberg et al.^[17] found that CPIS has a limited role both clinically and as a research tool.

Many diseases exhibit changes in leukocyte count and body temperature, which are part of the CPIS criteria. Aspiration pneumonia (chemical), pulmonary hemorrhage, lung contusion, and drug reaction should be considered in the differential diagnosis of VAP. Many patients in the ICU and in various disease groups, such as ARDS, sepsis, trauma, and burns, exhibit Systemic Inflammatory Response Syndrome (SIRS). Systemic findings are fever, tachycardia, and leukocytosis, as well as non-specific findings due to increased cytokines. Trauma, fever, leukocytosis, and sepsis present in the postoperative patient group complicate the clinician's job. It is clear that the exclusion of patients with sepsis in our study increased the efficacy of CPIS in the diagnosis of VAP. We believe that a CPIS value of 6 or more is not diagnostic alone in the light of our study. However, we believe that follow-up of patients with CPIS leads to early suspicion of VAP development and leads to early admission to the necessary diagnostic approach, thus providing a high clinical benefit. Patients with pulmonary edema, pulmonary infarction, devascularized tissue, and atelectasis may also exhibit fever and leucocytosis during the first 72 hours postoperatively. Research has demonstrated a weak CPIS efficacy in these patient groups.^[27] Postoperative patients make up 9.3% of our study group. 25% of these developed VAP, and 75% did not.

The largest prospective study conducted today is the study by the Canadian Intensive Care Working Group to measure the differential power of CPIS in VAP. In this multicentre study involving 739

patients, they investigated the utility of modified CPIS as a pre-test for the identification of VAP diagnoses. Of the 739 patients, they defined 107 (14.5%) as low, 293 (39.6%) as moderate and 339 (45.9%) as highly probable VAP. Of these patients, 625 (84.6%) were defined as VAP. However, ETA and BAL samples revealed proliferation in 341 (45.99%) patients. Therefore, we understand that CPIS serves as a preliminary test for VAP diagnosis, but it is not a definitive diagnostic tool on its own. Furthermore, researchers evaluate it as a complementary screening tool to antimicrobial treatment.^[26] In a study conducted by Sachder et al.^[28] in a pediatric ICU, modified CPIS was used in the follow-up of the patients, and they found that it helped to initiate the diagnostic procedure in the diagnosis of VAP [28].

The importance of early diagnosis of VAP in ICUs is crucial. The Clinical Pulmonary Infection Score (CPIS) provides close follow-up for intensive care patients and early suspicion of developing pneumonia. It is a method of warning the clinician and providing an application for the necessary diagnostic methods. In this regard, we believe that it will be a useful screening method in the follow-up of ICU patients.

Current studies suggest that serial CPIS measurements in patients under mechanical ventilation may be used to identify developing pneumonia that has not yet been clinically defined. Patients who receive improper treatment or delayed treatment with appropriate antibiotics differ in their mortality from those receiving adequate therapy.

Authorities believe that early initiation of appropriate treatment with guidance from CPIS or another clinical score guideline leads to improvements in the outcomes of VAP patients [23]. The rise of CPIS should be a warning for clinicians.

CONCLUSION

In our study, ETA cultures showed positive results on the day of CPIS increase. For this reason, it is possible to start early antibiotic therapy against the potential agent without waiting for the culture result, to repeated CPIS measurements. Serial CPIS measurements can help the clinician in early diagnosis and treatment of VAP. Differences in the morbidity and mortality of patients can be recorded with early treatment.

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